Procedure

(1) Prepare a coating solution containing Eudragit E and citric acid in water.
(2) Coat Isosorbide Mononitrate Enteric Coated CAT unit (step (B)) with the above coating solution in a coating pan or a fluid bed coater until a desired coating weight is obtained.

(D) Preparation of Nitroglycerin Semi-moist Triturate Blend:

Ingredients	% Weight	Typical Example mg/tablet
Nitroglycerin	0.2-5	0.3
Lactose, fine powder	70-95	65
Sucrose, fine powder	2-20	5
Flavoring agent	0.5-5	2
Polyvinylpyrrolidone	0.05-1	0.1
Ethyl alcohol, 95%	(To be evaporated)	—
Water	(To be evaporated)	—
Sub Total		72.4

Procedure

(1) Prepare the solvent mixture containing polyvinylpyrrolidone, ethyl alcohol and water.
(2) Blend Nitroglycerin, lactose, sucrose and the flavoring agent. Screen to break lumps.
(3) Add (1) to (2) until a moistened powder blend is achieved.

(E) Preparation of Molded Triturate Tablet into the CAT—The Finished Product (CAT/T)

Ingredients	% Weight	Typical Example mg/tablet
Isosorbide mononitrate Enteric Coated Sustained release CAT (B)	70-90	281.06
Nitroglycerin Triturate Blend (C)	10-30	72.4
Total (Finished product)		353.46

Procedure

Prepare the finished dosage form by pressing the semi-moist triturate blend (C) into the center cavity of the CAT(B) using an apparatus capable of molding triturate tablets into a CAT.

(F) Description of the Dosage Unit Design:

The product contains 0.3 mg nitroglycerin in the molded triturate tablet for intraoral release and 30 mg Isosorbide Mononitrate in the CAT as a sustained release form which releases Isosorbide for a duration of 8 to 12 hours. The Isosorbide sustained release CAT unit is further coated with delayed release formulation so that the sustained released Isosorbide CAT starts to release 1 to 2 hours after administration of the dosage form.

The patient is instructed to take the dosage unit intraorally where the molded triturate tablet disintegrates rapidly resulting in the rapid release of the drug for intraoral absorption. Once the disintegration of molded triturate tablet is complete the patient may swallow the remainder of the dosage unit, the CAT, which will then release Isosorbide Mononitrate 1 to 2 hours later for a sustained release duration of 8 to 12 hours. The initial immediate release of Nitroglycerin from the triturate provides a rapid onset to prevent acute angina attack due to coronary artery disease for a duration of about 30 minutes to 1 hour at which time the delayed and sustained release Isosorbide Mononitrate CAT starts to release and provides a duration of 8 to 12 hours therapeutic intervention for prophylactic effect for angina.

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What is claimed is:

1. A pharmaceutical composition which comprises:

(a) an intraorally first releasing portion, in the form of a tablet comprising a therapeutically effective amount of at least one pharmaceutically active ingredient capable of intraoral administration having a molecular weight of less than 350 Daltons, in a dosage of no more than 50 mg, wherein the tablet comprises an excipient and disintegrates or dissolves within 10 minutes permitting rapid release and uptake of the pharmaceutically active ingredient within the oral region; and

(b) a second releasing portion located around the first portion, comprising a therapeutically effective amount of at least one pharmaceutically active ingredient capable of oral administration and which is releasable and orally ingestible by the patient after the tablet of (a) has disintegrated or has dissolved intraorally wherein it is absorbed after swallowing.